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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/027,654	02/23/1998	JEFFREY KENNETH HORTON	28911/34561	3465

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EXAMINER
GABEL, GAILENE

ART UNIT	PAPER NUMBER
1641	19

DATE MAILED: 02/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/027,654	HORTON, JEFFREY KENNETH	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/26/01-CPA* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/18/02 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 1/18/02 in Paper No. 16 are acknowledged and have been entered. Claims 1, 17 and 18 have been amended. Claim 21 has been added. Currently, Claims 1-2, and 4-21 are pending and under examination.

Claim Objections

3. Claim 15 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 10. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Rejection Withdrawn

4. In light Applicant's argument, the rejection of claims 1-2, 4-5, 8-11, and 13-20 under 35 U.S.C. 103(a) as being unpatentable over Cook (1) (Research Focus, 1996) in view of Lundin (US 5,558,986), is hereby, withdrawn.

5. In light Applicant's argument, the rejection of claims 6-7 and 12 under 35 U.S.C. 103(a) as being unpatentable over Cook (1) (Research Focus, 1996) in view of Lundin (US 5,558,986), and in further view of Cook (2) (WO 94/26413), is hereby, withdrawn.

Rejection Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-2, 4-13, 15-19, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. Specifically, it is unclear how detection is performed in the absence of a label or a tracer. Throughout Applicant's specification, it appears that a label or tracer is required in detecting the analyte in question, regardless of what assay format is being utilized. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the

specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claims 14 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Lundin (US 5,705,345).

Lundin discloses a kit suitable for lysis and assay of analytes, i.e. ATP, comprising a lysis reagent (surfactant), cyclodextrin, specific binding partner, i.e. firefly luciferase reagents, an assay buffer, and a separation means, i.e. dipstick- separates bound from unbound tracers (see columns 7-8).

8. Claims 1-2, 4-5, 8, 10, 14-18, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Khanna (US 5,032,503).

Khanna et al. disclose a specific binding assay for determining the presence of analyte in a cell sample (whole blood) (see column 3, lines 11-20 and column 2, lines 50-54). Specifically, Khanna et al. disclose mixing the cell sample with a lysis reagent

or detergent (surfactant), specific binding partners for the analyte (anti-analyte antibody, enzyme-analyte conjugate), and cyclodextrin to initiate complex formation, whereby the presence of analyte and specific binding partner reaction is indicative of the presence of the analyte in the sample (see column 5, lines 12-32). Khanna et al. also disclose labeling the specific binding partners, i.e. fluorescer, enzyme (see column 3, lines 21-40). Khanna et al. disclose using dodecyltrimethylammonium bromide as a detergent for the assay (see column 3, line 41 to column 4, line 4). Specifically, Khanna et al. disclose using cyclodextrin in a sufficient amount to neutralize the detergent and allow complex formation between the specific binding partners. Cyclodextrin concentrations including an amount of 1-5% of the reaction mixture is set forth in column 4, lines 37-58. Khanna et al. also disclose a kit suitable for diagnostic immunoassay of the analytes comprising a lysis detergent, cyclodextrin, specific binding partners, assay buffers, drying agents, and excepients, i.e. to remove materials as in unbound tracers (see column 7, lines 37-60).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 7, 11-13, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khanna (US 5,032,503) in view of Brown et al. (US 5,739,001).

Khanna et al. has been discussed supra. Khanna et al. differ in failing to disclose that the cells are cultured, lysed, and assayed in a vessel and in the presence of the culture medium. Khanna et al. further differ in failing to disclose assaying for cyclic AMP and separating bound from unbound tracers.

Brown et al. disclose a specific binding assay (cell-based assay) for determining the presence of cell-related analyte in a cell sample. Specifically, Brown et al. disclose mixing the cell sample (whole blood) with a lysis reagent to lyse red blood cells in the sample. Brown et al. also disclose mixing the lysed cellular sample with a specific binding partner for the analyte, i.e. anti-LTC_4 antibody for Leukotriene C_4, in order to form analyte-specific binding partner complexes whereby the presence of analyte and specific binding partner complexes is indicative of the presence of the analyte in the sample. See Example 2 and column 3, lines 18-42. Other analytes that can be detected using this method include adenosine-3', 5'- cyclic monophosphate (cyclic AMP) and cytokines, i.e. interleukin-6 (see column 4, lines 59-64). Brown et al. disclose that the assay is a homogeneous assay that is performed in a single reaction vessel (cells are not attached to solid phase for assay) (see column 4, lines 5-12 and lines 38-56). The cells are cultured, lysed, and assayed in the same vessel; thus, eliminating the need for a separate culturing step (see column 3, line 66 to column 4, line 1). The specific binding partners can be immune type, i.e. antibody or non-immune type, i.e. biotin/avidin (see column 5, lines 12-38). Brown et al. also disclose labeling the specific binding partner with a tracer or label, i.e. ^{3}H and ^{125}I (see column 6, lines 5-16).

One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Brown in culturing, lysing, and assaying for intracellular analyte such as cyclic AMP in a single reaction vessel, into the cell-based immunodiagnostic assay taught by Khanna because Brown's method provides a capability to detect both intracellular and cell-surface analytes and their functions, from samples grown in a cell culture medium in a single reaction vessel; thus, eliminating the need for a separate "culturing step" that would have been otherwise required.

10. Claims 6 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khanna (US 5,032,503) in view of Cook (2) (WO 94/26413).

Khanna et al. have been discussed supra. Khanna et al. differ from the instant invention in failing to teach a multiwell plate. Khanna et al. further differ in failing to teach scintillation proximity assay.

Cook (2) discloses an apparatus and method for studying cellular processes using scintillation proximity assay. The apparatus comprises a vessel having a base with a scintillant substance and which is adapted for attachment and growth of cells (see Abstract). Cook (2) further discloses a multiwell plate comprising an array of wells held in fixed relationship to one another wherein each well is a vessel (see page 10, first full paragraph). The scintillant substance include aromatic hydrocarbons which emit light used for detection. The method of studying cellular processes includes introducing into the vessel a sample of cells labeled with a radioisotope emitting electrons, and using detection means to observe scintillation caused by radioactive decay so as to

study the cellular process (see page 10, second full paragraph). The multiwell plate can take various formats for the purpose of culturing cells using standard cell culture media and growing cells in a sterile environment at 37 C in a 95 % humidified air and 5% CO2 incubator as well as studying cellular biochemical processes in living cells (page 14, second and third full paragraphs and page 15, second full paragraph). Cook (2) disclose that the surface of wells or vessels in the microwell plate requires modification in order to be adapted for the attachment and/or growth of cells. Cook (2) disclose that a considerable advantage of the scintillation proximity assay is that it does not require separation of bound and molecular species from free, thereby minimizing handling of potentially hazardous substances (see page 7, second full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the scintillation proximity multiwell assay system having an array of reaction vessels as taught by Cook (2) into the cell-based immunodiagnostic assay taught by Khanna because the system taught by Cook (2) provides advantage in minimal handling of materials in high-throughput immunoassay testing of a plurality of live culture cells, in order to screen for cellular analytes, functions, and processes. One of ordinary skill in the art would have been motivated to incorporate the derivatized multiwell system of Cook (2) into the method of Khanna because of the high throughput capacity achieved in simultaneously assaying for identification of a wide variety of biochemical and cellular analytes.

11. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Khanna (US 5,032,503) in view of Edmonds (US 6,159,750).

Khanna et al. has been discussed supra. Khanna et al. differ from the instant invention in failing to teach that the specific binding assay is fluorescence polarization assay.

Edmonds discloses a specific binding assay for the detection of analytes, i.e. T4 hormone and Free Estriol, wherein reagents, i.e. antibodies or specific binding partners and labels, are mixed with the sample containing the analyte and are caused to react. Edmonds discloses using fluorescence polarization assay to detect and measure the concentration of the analyte in the sample. See Abstract, Example 2, and Example 4.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to detect the polarization characteristics of the specific binding assay taught by Khanna using fluorescence polarization assay as taught by Edmonds because Khanna is generic with respect to the type of detection used in detecting the presence and amount of the analyte and Edmonds specifically taught that fluorescence polarization immunoassay is a common and conventional method of analyzing samples for the presence of analyte of interest.

Response to Arguments

12. Applicant's arguments with respect to claims 1-2 and 4-21 have been considered but are moot in view of the new grounds of rejection. Accordingly, no claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gail Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gail Gabel
Patent Examiner
Group 1641

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